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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/395,677	09/10/1999	DOLORES M. BERGER	P-4579	6334

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EXAMINER

FORMAN, BETTY J

ART UNIT

PAPER NUMBER

1634

DATE MAILED: 05/30/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	09/395,677	BERGER ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	BJ Forman	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 14 March 2003.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 13,14,16,18,19,21-23 and 25-32 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 13,14,16,18,19,21-23 and 25-32 is/are rejected.
- 7) ☒ Claim(s) 13 and 19 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).  
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                             | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____  |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)         | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____                                    |

**DETAILED ACTION**

***Continued Examination Under 37 CFR 1.114***

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 14 March 2003 has been entered.

2. This action is in response to papers filed 14 March 2003 in which claims 13, 19, 21 and 22 were amended and claims 15, 20 and 24 were canceled. All of the amendments have been thoroughly reviewed and entered.

The previous rejections in the Office Action dated 11 April 2002 are withdrawn in view of the amendments.

All of the arguments have been thoroughly reviewed but are deemed moot in view of the amendments, withdrawn rejections and new grounds for rejections.

New grounds for rejection are discussed.

Claims 13-14, 16, 18-19, 21-23 and 25-32 are under prosecution.

***Claim Objections***

3. Claims 13 and 19 are objected to because of the following typographical errors:

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- a. Claim 13, step (ii), line 5, "substance" is misspelled "substances".
- b. Claim 19, line 2, "substance" is misspelled "substances".

Appropriate correction is required.

***Claim Rejections - 35 USC § 102/103***

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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6. Claims 13, 14, 16, 21, 23, 25, 26, 28-31 are rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Rogers (U.S. Patent No. 6,232,092 B1, filed 2 October 1998).

Regarding Claim 13, Rogers teaches a method for stabilizing the nucleic acids of at least one cell in a sample comprising; adding to a vessel containing the sample a composition comprising a first substance having a concentration effective for denaturing proteins comprising at least one alcohol or ketone whose concentration is 80% of the total composition; and a second facilitator substance having a concentration effective for aiding the infusion of the first substance into said at least one cell whose concentration is 20% of the total composition; contacting said at least one cell in said sample with said composition; incubating said sample with said composition for an effective period of time and at an effective temperature; and obtaining at least one cell with stabilized nucleic acids in said sample (Column 4, lines 8-15 and 40-50 and Column 5, lines 61-66).

The preceding rejection is based on judicial precedent following *In re Fitzgerald*, 205 USPQ 594 because Rogers is silent with regard to the alcohol being greater than 80% and the DMSO being less than 20%. However, the greater than 80% and less than 20% recited in Claim 1 is deemed to be inherent in the composition of Rogers because the claims encompass alcohol at 80.00000000.....1% and DMSO at 19.999999999999999...9%. The composition of Rogers would inherently fall within the limitations of the claims because any compositions measured and mixed in a laboratory would differ due to a margin of error in measurement and/or evaporation and/or spillage. Therefore, the compositions prepared using the method of Rogers would inherently produce a composition comprising first and second substances having concentrations of less than 80% and greater than 20 % respectively.

Alternatively, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to adjust the composition concentrations of Rogers using routine experimentation to thereby derive an optimal composition for stabilizing cellular

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nucleic acids because the skilled practitioner in the art would have been motivated to optimize the composition to thereby maximize stabilization. It is noted that *In re Aller*, 220 F.2d 454,456, 105 USPQ 233,235 states where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum by routine experimentation.

Regarding Claim 14, Rogers teaches the method wherein the at least one alcohol is selected from the group consisting of ethanol and methanol (Column 4, lines 40-42).

Regarding Claim 16, Rogers teaches the method wherein the first substance is comprised of one alcohol (Column 5, lines 61-66).

Regarding Claim 21, Rogers teaches the method wherein the first substance is methanol and the second substance is dimethyl sulfoxide (Column 5, lines 61-66).

Regarding Claim 23, Rogers teaches the method wherein the first substance is ethanol (Column 4, lines 40-42).

Regarding Claim 25, Rogers teaches the method wherein the nucleic acid is DNA (Column 4, lines 8-15).

Regarding Claim 26, Rogers teaches the method wherein the nucleic acid is RNA (Column 4, lines 8-15).

Regarding Claim 28, Rogers teaches the effective time is **about** one day (Column 5, lines 61-67).

Regarding Claim 29, Rogers teaches the effective temperature is room temperature (Column 5, line 67-Column 6, line 2).

Regarding Claim 30, Rogers teaches the effective temperature is from 0° C to 40° C i.e. room temperature (Column 5, line 67-Column 6, line 2).

Regarding Claim 31, Rogers teaches the cell is a eukaryote (Column 4, lines 16-24).

#### **Response to Arguments**

7. Applicant argues that Rogers is improperly cited as prior art because Rogers is concerned with methods to clarify and contrast stain tissue samples and therefore one of skill

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in the nucleic acid stabilization art would not logically consider fixative for microscopy in considering an answer to a molecular problem. The argument has been considered but is not found persuasive because Rogers teaches the claimed method steps. The fact that Rogers utilizes the method steps for tissue examination does not negate the fact that Rogers teaches the claimed method.

In response to applicant's argument that Rogers is nonanalogous art, it has been held that a prior art reference must either be in the field of applicant's endeavor or, if not, then be reasonably pertinent to the particular problem with which the applicant was concerned, in order to be relied upon as a basis for rejection of the claimed invention. See *In re Oetiker*, 977 F.2d 1443, 24 USPQ2d 1443 (Fed. Cir. 1992). In this case, the instant claims and the method of Roger concern cellular stabilization and examination of cellular components (see Rogers, Column 4, lines 8-15). As such, the claims and the teaching of Rogers are analogous art.

Applicant further argues that Rogers is not limited to methanol and DMSO but includes very low temperatures (-70° C), gentle agitation, application of a vacuum in cycles, use of hydrogen peroxide, use of 100% methanol, use of pigment, use of a benzyl alcohol/benzyl benzoate solution, mounting, use of fresh BABB solution and viewing the specimen under a microscope. The argument has been considered but is not found persuasive because the claims are drawn to a method "comprising" steps (a) through (d). The open claim language "comprising" encompasses the additional steps of Rogers.

***Claim Rejections - 35 USC § 103***

8. Claims 18, 19 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rogers (U.S. Patent No. 6,232,092 B1, filed 2 October 1998) in view of Essenfeld et al (U.S. Patent No. 6,207,408 B1, filed 19 August 1998).

Regarding Claims 18, 19 and 22, Rogers teaches a method for stabilizing the nucleic acids of at least one cell in a sample comprising; adding to a vessel containing the sample a composition comprising a first substance having a concentration effective for denaturing proteins comprising at least one alcohol or ketone whose concentration is 80% of the total composition; and a second facilitator substance having a concentration effective for aiding the infusion of the first substance into said at least one cell whose concentration is 20% of the total composition; contacting said at least one cell in said sample with said composition; incubating said sample with said composition for an effective period of time and at an effective temperature; and obtaining at least one cell with stabilized nucleic acids in said sample (Column 4, lines 8-15 and 40-50 and Column 5, lines 61-66). Rogers does not teach the first substance is an alcohol and a ketone (Claim 18), wherein concentrations of the first substance and DMSO are 2.5 : 2.5 : 5 (Claim 19) and wherein the first substance comprises ethanol and methanol (Claim 22).

Essenfeld et al teach a similar a method for stabilizing the nucleic acids of at least one cell in a sample comprising; adding to a vessel containing the sample a composition comprising a first substance (Column 5, lines 28-33) having a concentration effective for denaturing proteins comprising at least one alcohol or ketone whose concentration is less than 80% of the total composition; and a second facilitator substance (Column 5, lines 17-27) having a concentration effective for aiding the infusion of the first substance into said at least one cell whose concentration is greater than 20% of the total composition; contacting said at least one cell in said sample with said composition; incubating said sample with said composition for an effective period of time and at an effective temperature; and obtaining at least one cell with



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stabilized nucleic acids in said sample (Column 10, lines 8-13 Example 1, Column 16, lines 13-45 and Claim 13) wherein the first substance comprises two alcohols (Examples 1-3) and wherein the alcohols are methanol and ethanol (Column 5, lines 27-33).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the alcohol of Rogers by utilizing two alcohols as taught by Essenfeld based on the preference of two alcohol stabilization taught by Essenfeld (Examples 1-3). Furthermore, one of skill in the art would have been motivated based on the two alcohol teaching of Essenfeld to adjust the concentration ratios of the alcohols using routine experimentation to thereby optimize experimental conditions and maximize experimental results. It is noted that *In re Aller*, 220 F.2d 454,456, 105 USPQ 233,235 states where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum by routine experimentation.

9. Claims 27 and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rogers (U.S. Patent No. 6,232,092 B1, filed 2 October 1998).

Regarding Claim 27, Rogers teaches a method for stabilizing the nucleic acids of at least one cell in a sample comprising; adding to a vessel containing the sample a composition comprising a first substance having a concentration effective for denaturing proteins comprising at least one alcohol or ketone whose concentration is 80% of the total composition; and a second facilitator substance having a concentration effective for aiding the infusion of the first substance into said at least one cell whose concentration is 20% of the total composition; contacting said at least one cell in said sample with said composition; incubating said sample with said composition for an effective period of time and at an effective temperature; and

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obtaining at least one cell with stabilized nucleic acids in said sample (Column 4, lines 8-15 and 40-50 and Column 5, lines 61-66) wherein the nucleic acids are DNA and/or RNA (Column 4, lines 8-15) but they do not specifically teach the RNA is ribosomal RNA. However, RNA and ribosomal RNA are structurally, functionally and chemically equivalent. Therefore, one of ordinary skill in the art would have been motivated to stabilize ribosomal RNA along with the RNA and/or DNA based on their structural, functional and chemical equivalence.

The courts have stated with regard to chemical homologs that the greater the physical and chemical similarities between the claimed species and any species disclosed in the prior art, the greater the expectation that the claimed subject matter will function in an equivalent manner (see *Dillon*, 99 F.2d at 696, 16 USPQ2d at 1904).

Regarding Claim 32, Rogers teaches the cell is a eukaryote (Column 4, lines 16-24) but they do not specifically teach the cell is a microorganism. However, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the cell fixation of Rogers to cellular microbes within their tissue samples based on the teaching of Rogers wherein their method is utilized to analyze surrounding foreign material (Abstract).

### **Conclusion**

10. No claim is allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (703) 306-5878. The examiner can normally be reached on 6:30 TO 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this

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application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-8724 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



BJ Forman, Ph.D.  
Patent Examiner  
Art Unit: 1634  
May 29, 2003